

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (**Currently Amended**) A modified Staphylococcal enterotoxin B (SEB) having a reduced reactivity with a neutralizing antibody to SEB (anti-SEB antibody) and being soluble in water.

2. (**Original**) The modified SEB of claim 1 wherein the reactivity with the anti-SEB antibody was reduced by introducing arbitrary amino acid substitution in the amino acid sequence of SEB.

3. (**Original**) The modified SEB of claim 2 wherein the amino acid substitution was introduced at an epitope recognition site of the anti-SEB antibody in the amino acid sequence of SEB.

4. (**Currently Amended**) The modified SEB of claim 2 wherein the amino acid substitution was introduced within a region from Lys at 226-position to Lys at 229-position in the amino acid sequence of SEB as shown in SEQ ID NO: 1.

5. **(Currently Amended)** The modified SEB of claim 4 wherein the amino acid sequence of from 226-position to 229-position in the amino acid sequence of SEB as shown in SEQ ID NO: 1 is Leu Phe Ala Ala.

6. **(Currently Amended)** The modified SEB of claim 4 wherein the amino acid sequence of from 226-position to 229-position in the amino acid sequence of SEB as shown in SEQ ID NO: 1 is Ala Thr Thr Gln.

7. **(Currently Amended)** The modified SEB of claim 4 wherein the amino acid sequence of from 226-position to 229-position in the amino acid sequence of SEB as shown in SEQ ID NO: 1 is Lys Arg Ile Ile.

8. **(Currently Amended)** The modified SEB of claim 1 wherein Asn at 23-position in the amino acid sequence of SEB as shown in SEQ ID NO: 1 is substituted with Tyr.

9. **(Currently Amended)** A ~~prophylactic/remedy~~ treatment composition comprising

as an active ingredient the modified SEB as set forth in claim 1,

wherein said ~~prophylactic/remedy~~ treatment composition provides a reduced immunological response to SEB and an inhibitory activity to T cell activation,

said ~~prophylactic/remedy~~ treatment composition being in a form adapted for immunopathy.

Claim 10 (**Cancelled**).

11. (**Currently Amended**) The ~~prophylactic/remedy~~ for immunopathy of claim 22 ~~claim 9 or 10~~ wherein said form is a form for oral administration.

12. (**Currently Amended**) The modified SEB of claim 2 wherein Asn at 23-position in the amino acid sequence of SEB as shown in SEQ ID NO: 1 is substituted with Tyr.

13. (**Currently Amended**) The modified SEB of claim 3 wherein Asn at 23-position in the amino acid sequence of SEB as shown in SEQ ID NO: 1 is substituted with Tyr.

14. (**Currently Amended**) The modified SEB of claim 4 wherein Asn at 23-position in the amino acid sequence of SEB as shown in SEQ ID NO: 1 is substituted with Tyr.

15. **(Currently Amended)** The modified SEB of claim 5 wherein Asn at 23-position in the amino acid sequence of SEB as shown in SEQ ID NO: 1 is substituted with Tyr.

16. **(Currently Amended)** The modified SEB of claim 6 wherein Asn at 23-position in the amino acid sequence of SEB as shown in SEQ ID NO: 1 is substituted with Tyr.

17. **(Currently Amended)** The modified SEB of claim 7 wherein Asn at 23-position in the amino acid sequence of SEB as shown in SEQ ID NO: 1 is substituted with Tyr.

Claims 18-20 **(Cancelled)**.

21. **(Currently Amended)** A modified Staphylococcal enterotoxin B (SEB) having a reduced reactivity with a neutralizing antibody to SEB (anti-SEB antibody),

capable of being expressed in a soluble form in E. coli to be maintained stably in an aqueous solution and that retains a therapeutic effect to immunopathy equivalent to that of naturally occurring SEB,

wherein the reactivity with anti-SEB antibody is reduced by introducing in the amino acid sequence of SEB as shown in SEQ ID NO: 1 an amino acid substitution from Lys at 226-position to

Lys at 229-position of Leu Phe Ala Ala, Ala Thr Thr Gln or Lys Arg

Ile Ile, and

wherein Asn at 23-position is substituted with Tyr.

22. (New) A remedy comprising the modified SEB mutant N23Y or 47C7 or 4C1 wherein said mutants have reduced binding to an anti-SEB antibody and wherein said mutants produce inhibitory cytokines at higher levels compared to the production of inflammatory cytokines as compared to wild type SEB for treatment of rheumatoid arthritis.

23. (New) In a method for the treatment of rheumatoid arthritis comprising administration to a patient in need thereof an effective amount of a treatment agent, the improvement wherein the treatment agent comprises the modified SEB of claim 21.